REMARKS

Reconsideration and withdrawal of the rejections of the claimed invention is respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-3, 6-8 and 11-25 are now pending in this application. In order to expedite prosecution, the applicants have amended claim 1 to define the amount of capsaicin/capsaicin analog and amount and type of amphiphilic solvent has been added. Support for these amendments can be found throughout the specification, e.g., see paragraphs [0015] and [0039] of the specification. New claim 24 is supported by the data in Table 2 and 3 of the specification. No new matter has been added by this amendment.

The applicants request reconsideration of their response from 25 February 2010 (and additional comments) below in light of the claims as amended.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112.

II. THE 35 U.S.C. 112, 1st PARAGRAPH REJECTION HAS BEEN OVERCOME

Claims 1-23 were rejected as allegedly lacking adequate written description without providing any factual evidence in support of her position as relating to the issue at hand, i.e. the possession of capsaicin analogs. The numerous case law citations in the Office Action is simply not relevant here as the facts of the cited decisions were not directed to compounds/composition which have any similarity to capsaicin analogs.[1]

The applicants previously rebutted the Examiner's rejection in their 25 February 2010 response for failing to possess the use of capsaicin analogs at the time the invention was filed with at least as much factual evidence as provided by the Examiner. As such, at best for the Examiner, the respective positions are in equipoise and therefore insufficient to establish a *prima facie* case of lacking written description for capsaicin analogs.

[1] MPEP 2144.04 states that "...if the facts in a prior legal decision are sufficiently similar to those in an application under examination, the examiner may use the rationale used by the court."

However, the applicants further relied upon Robbins (U.S. Patent 6,239,180) to show that one of ordinary skill in the art would acknowledge possession, know the meaning and be able to determine the scope of a capsaicin analog as Robbins not only used the term in the specification, but also in their claims. Moreover, the applicants describe in several locations in their specification that the use a capsaicin or a capsaicin analog is used as therapeutic compound or in the treatment of pain (see paragraphs [0002] and [0005] of the publication of the application); as such, one of ordinary skill in the art would be able to determine the nature of a capsaicin analog based on the known structure of capsaicin as well as its known use which is further established by Robbins.

(The applicants provide the text of their previous response from 25 February 2010 filing below as the holding of lack of written description was never reestablished by the response in the 2 June 2010 Office Action):

The claims were rejected for the applicants' use of terms "capsaicin analog". However, this term is not only part of the applicants' specification, but also the originally filed claims. It is well known that there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims"); *See also* MPEP 2163, section II. A.

Moreover, the Office Action cited U.S. Patent 6,239,180 ("Robbins '180") in the obviousness and obviousness-type double patenting rejections which are addressed in greater detail in sections III. and IV. below.

Robbins '180 and Robbins (U.S. Patent 6,248,788) are both described in the applicants' background section of the specification (see paragraph [0002] of the publication of this application). Robbins '180 not only refers to "capsaicin analogs" throughout their specification, but it is also part of their claims (see e.g. claims 1 and 3). As such, one of ordinary skill in the capsaicin arts is apprised of the meaning and scope of the term capsaicin analog and would have presumed that the applicants and Robbins had possession of the concept of capsaicin analog absent any evidence to the contrary.

Lastly, the applicants note that maintaining this rejection is an implicit rejection of the allowed claims of Robbins '180. However, each claim of a patent is presumed to be valid. *See* 35 U.S.C. 282. As such, maintaining this rejection is casting aspersions on a previously issued U.S. patent which is explicitly not permitted. MPEP 1701 - Office Personnel Not to Express Opinion on Validity or Patentability of Patent.

III. THE 35 U.S.C. 103(a) REJECTION HAS BEEN OVERCOME

Claims 1-23 were rejected as allegedly being obvious by Müller (WO 01/01967) in view of Robbins (US 6,239,180 – "Robbins") and Schacht et al. (US 2005-0079206 -"Schacht"). The applicants request reconsideration of this rejection for the following reasons.

WO 01/01967 is the publication of the PCT application which resulted in U.S. Application Serial No. 10/835,997 ("the '997 application"), which is subject to the obviousness-type double patenting rejection addressed in section IV. below. Dr. Walter Müller is the named inventor in both WO 01/01967 and the present application.

A. Allowability of species inventions over the genus invention

During the 8 December 2009 interview between the Examiner and the applicants' representative (Howard C. Lee), it appeared a general agreement was reached that this application represented a "species" invention in relation to the "genus" represented by the '997 application, i.e. whereas both application are directed toward the use of microreservoirs with amphiphilic solvents, the present application is specifically directed toward capsaicin and capsaicin analogs instead of being generically directed to therapeutic compounds.

It was also noted during the interview that the applicants have already received a "species" patent wherein the therapeutic compound was fentanyl (see U.S. Patent 7,390,500 – "the '500 patent"). As such, the applicants were confused by the nature of the rejection for this application (as well as the genus application) as the rejection appears to be revisiting old issues which have already been decided, i.e. the Examiner in the '500 patent also considered WO 01/01967 and the fentanyl claims in the '500 patent were allowed.

For the claims as amended, the nature of the solvent system AND the nature of active ingredients would both be considered species with the genus.

B. No rationale for combining WO 01/01967 with Robbins and Schacht

In order to establish a prima facie case of obviousness, both the applicants' claimed invention and the cited references must be considered as a whole. While this does not preclude the use of any part of the cited reference, the overall teaching of the reference must be considered as well.

The Office Action stated that it would have been obvious to "...replace the analgesic agent with capsaicin or capsaicin analog taught by Robbins." (see page 10, lines 6-7 of the Office Action). WO 01/01967 is generic for therapeutic compounds, but Robbins does not provide the requisite teaching or suggestion to combine capsaicin or capsaicin analog into the applicants' topical patch not only for the reason of unexpected results which is described below in section C., but because Robbins is directed toward a fundamentally different invention.

Robbins clearly requires an anesthetic in combination with their invention which is not a required element of the present invention. ("Transdermal application of capsaicin (or a capsaicin analog) in a concentration from greater than about 5% to about 10% by weight has been discovered to be an extremely effective therapy for treating neuropathic pain, ***so long as an anesthetic***, preferably by means of a transdermal patch, is administered initially to the affected area to minimize the expected side effect from subsequent capsaicin application." - see Abstract of Robbins (emphasis added))

Moreover, Robbins cannot even contemplate that high concentrations of capsaicin is even possible without an anesthetic ("Because the patient in the following example describes long term pain relief much beyond the expected duration of the regional anesthetic, this relief cannot be due to the action of the anesthetic alone and is due to the combination of the block and capsaicin (***since administration of the high concentration capsaicin without the anesthetic would not be possible***)." – see col. 4, lines 45-52 (emphasis added)).

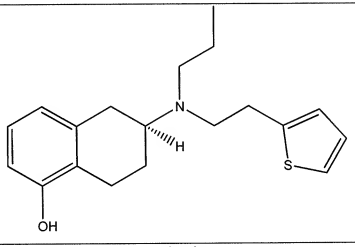
Therefore, Robbins does not suggest the replacing of capsaicin as the therapeutic compound, but a combination of capsaicin ***and*** an anesthetic as the therapeutic compound, i.e. even if one of ordinary skill in the art was limited to considering only the substitution of a single compound with another compound, such a selection would present an virtually an infinite number of possible solution to the problem of delivery of an analgesic.

However, if Robbins is considered to be relevant art, the selection by the skilled artisan would be for an even greater number of possible solutions, i.e. multiple compound combinations

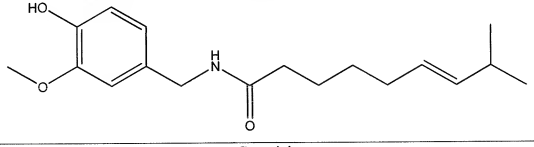
would then have to be considered as is suggested by Robbins as well as single compound substitutions and if multiple compound combinations are contemplated, no evidence has been presented as to why such combinations should be limited to just the two components as in Robbins (why not 3, 4, 5…100 or more?).

The Office Action also stated that it would have been obvious to "…provide [a] transdermal patch comprising polysiloxane matrix containing microreservoirs comprising capsaicin or its analogs dissolved in an amphiphilic solvent as taught by the combined teaching of Muller and Robbins, and replace the polysiloxane matrix with a matrix comprising mixture of high tack polysiloxane and medium tack polysiloxane as taught by Schacht." (see page 10, lines 14-19 of the Office Action).

However, when considering Schacht as a whole, it is clear that Schacht is specifically directed toward addressing the difficulties associated with rotigotine which is structurally and functionally different than capsaicin (see figures and functions below):



Rotigotine
(psychoactive drug for treatment of Parkinson's disease)



Capsaicin
(topical analgesic)

Schacht makes no assertions about other therapeutic compounds besides rotigotine. The teaching of Schacht attempted to address the problem associated with rotigotine with regard to keeping the compound in free base form, i.e. minimizing the amount of salt form, and keeping the rotigotine solubilized (hence, the suggested use of crystallization inhibitors) which is not a problem in the present invention because the capsaicin is dissolved in the microreservoir.

As such, one of ordinary skill in the art would not have been directed to taking the isolated element of a mixture of high tack polysiloxane and medium tack polysiloxane as taught by Schacht for use of a rotigotine delivery system into a topical patch for capsaicin or a capsaicin analog. Moreover, there is even some doubt that Schacht is even effective for their own teachings (see entry for rotigotine in Wikipedia attached to the end of the 25 February 2010 response – "As of 2008, Schwarz Pharma has recalled all Neupro (rotigotine) patches in the United States and some in Europe because of problems with the delivery mechanism.").

Therefore, when considering WO 01/01967, Robbins and Schacht as a whole, there is no direction to piece the disparate parts relied upon to arrive at the applicants' claimed topical patch which is directed to capsaicin and capsaicin analogs.

C. Combination of WO 01/01967, Robbins and Schacht does not suggest that capsaicin/microreservoir system would have a permeation rate which is double that of a system without microreservoirs and that long lasting pain relief was achieved with even minimal application times (Applicants have shown evidence of unexpected results)

Determinations of obviousness also requires consideration of any evidence of secondary considerations. Here, the applicants have shown that a topical patch of the invention has a permeation rate which is twice that of a topical patch which does not have the applicants' claimed microreservoir system where DGME is used as the solvent (see data from Tables 2 and 3 of the applicants' specification). Neither Robbins not Schacht would have predicted this unexpected permeation rate for capsaicin in the claimed topical patch. Moreover, as noted in paragraph [0041] of the publication of the application "...even a one-hour treatment of the affected areas reduced the sensation of pain significantly, ***the action lasting weeks***.". Nothing within WO 01/01967, Robbins and Schacht would have suggested that such a patch with capsaicin or an analog thereof could produce such a long lasting effect with such a short application time; at best the combination of WO 01/01967, Robbins and Schacht would only

show that long lasting effects could only be achieved via long lasting application of their respective patches.

Therefore, one of ordinary skill in the art would have found both the permeation rates and long lasting effects exhibited by the applicants to have been unexpected and a strong indicia of unobviousness.

IV. THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION HAS BEEN OVERCOME

Claims 1-23 have been provisionally rejected under obviousness-type double patenting over claims 32-55 of co-pending Application No: 10/835,997 in view of Robbins (US 6,239,180 - "Robbins"). While the secondary reference used to support this reject has changed from Holt (US 6,348,501) to Robbins, the main argument previously presented by the applicants still applies, i.e. while there are certain similarities between the analysis for an obviousness rejection and an obviousness-type double patenting (ODP) rejection, the rejections are not the same, i.e. the analysis for an ODP rejection is limited to a comparison of the respective claims and does not allow for the use of secondary references except for explanatory purposes (e.g. defining the meaning of a claim term). *See MPEP 804.*

However, in the present case, Robbins is being used to address a missing element of the applicants' claim. Therefore, the use of the Robbins is *prima facie* evidence that a basis for ODP does not exist and this rejection should be withdrawn. Moreover, even if Robbins had been an appropriate reference for use, Robbins was specifically directed to capsaicin and capsaicin analogs; it is not instructive of selecting capsaicin and capsaicin analogs from a generic teaching of a therapeutic compound or was predictive of the fact that the permeation rate of capsaicin and capsaicin analogs could be doubled (i.e. a showing of "unexpected results" as referred to above in section III.C.) by the use of microreservoirs of amphiphilic solvent in the matrix of the topical patch.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,
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